



## RAPID RISK ASSESSMENT

# Zika virus epidemic in the Americas: potential association with microcephaly and Guillain-Barré syndrome

10 December 2015

### Main conclusions

A Zika virus outbreak in the Americas and the South Pacific is evolving rapidly, and its spread is likely to continue as the vector species *Aedes aegypti* and *Aedes albopictus* are widely distributed there. While a significant increase in the number of newborns presenting with a low head circumference seems established in the north-eastern states of Brazil, the magnitude of the increase cannot be precisely estimated. Similarly, a link with Zika virus infection cannot be confirmed until the ongoing investigations are completed.

In the light of the current disease trend – and the possible association with severe complications – public health authorities in EU/EEA Member States should consider the following mitigation options:

- Enhance vigilance towards the detection of imported cases of Zika virus infection in EU Member States, EU Overseas Countries and Territories, and EU Outermost Regions, in particular where vectors or potential vectors are present, in order to reduce the risk of autochthonous transmission.
- Strengthen laboratory capacity to confirm suspected Zika virus infections in the European region in order to differentiate Zika virus infections from other arboviral infections (e.g. dengue, chikungunya).
- Blood safety authorities should consider the deferral of donors with a relevant travel history to areas with active Zika virus transmission, in line with measures defined for dengue virus.
- Increase awareness of clinicians and travel health clinics about the evolution of the Zika virus outbreak and the endemic areas so that they can include Zika virus infection in their differential diagnosis for travellers from those areas. Fever and/or macular or papular rash not attributable to dengue or chikungunya infection among travellers returning from areas currently experiencing a Zika virus outbreak should be considered indications for further investigation of Zika virus infection.
- Advise residents and travellers visiting affected areas, particularly pregnant women, to take individual protective measures to prevent mosquito bites all day round as Zika virus disease, chikungunya and dengue are transmitted by a daytime-biting mosquito. Consequently, protective measures should be taken, especially during the day.
- Ensure that Zika virus-infected patients in areas with *Aedes* mosquitoes avoid getting bitten during the first week of illness (mosquito net, screened doors and windows as recommended by WHO/PAHO).
- Increase awareness among health professionals who provide prenatal care of the possible association of Zika virus and microcephaly and adapt prenatal monitoring in accordance with the level of exposure to the vector.

## Source and date of request

ECDC internal decision on 3 December 2015; request from the European Commission on 4 December 2015.

## Public health issue

This document assesses the risks associated with the evolving Zika virus epidemic in the Americas, and in particular the possible association between Zika virus infection and congenital microcephaly; the association between Zika virus infection and Guillain–Barré syndrome; and other severe outcomes possibly linked to the disease. We further assess the potential risks associated with Zika virus infection for travellers to affected areas.

Previous ECDC rapid risk assessments on Zika virus outbreaks:

- 'Zika virus infection outbreak, French Polynesia', 14 February 2014 [1];
- 'Zika virus infection outbreak, Brazil and the Pacific region', 25 May 2015 [2];
- 'Microcephaly in Brazil potentially linked to the Zika virus epidemic', 24 November 2015 [3].

Detailed information on the epidemiology of the Zika can be found in an ECDC factsheet for health professionals [4].

## Consulted experts

ECDC internal response team in alphabetical order: Kaja Kaasik Aaslav, Sergio Brusin, Denis Coulombier, Niklas Danielsson, Dragoslav Domanovic, Romit Jain, Thomas Mollet, Joana Revez, Bertrand Sudre, Wim Van Bortel and Hervé Zeller.

Consulted external experts and acknowledgements. The following experts contributed to this risk assessment:

- WHO Regional Office for Europe, WHO Regional Office for America/Pan American Health Organization and World Health Organization Regional Office for the Western Pacific
- Fernando Bozza, MD, PhD, National Institute of Infectious Disease, Oswaldo Cruz Foundation, ministry of health, Rio de Janeiro, Brazil
- Vanessa Field, National Travel Health Network and Centre (NaTHNaC), Public Health England.

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## Disease background information

### Zika virus disease

Zika virus disease is a mosquito-borne viral disease caused by the Zika flavivirus [5]. There are two main lineages of Zika virus, the African lineage and the Asian lineage [6-8].

The disease symptoms are usually mild and last for 2 to 7 days. Infection may go unrecognised or be misdiagnosed as dengue, chikungunya or other viral infections giving fever and rash. Asymptomatic infections are common, as described with flaviviral infections such as dengue and West Nile fever, and only one in four people infected with Zika virus are believed to develop symptoms [9,10].

An association with Guillain–Barré syndrome (GBS) and other autoimmune neurological complications was suspected during the 2013–2014 outbreak in French Polynesia and remains under investigation [11-14].

There is some evidence that mother-to-child transmission can occur, most probably transplacental or during the delivery of a viraemic mother [15]. On 2 December, the National Institute of Women's Health, Child and Adolescent Fernandes Figueira, the Oswaldo Cruz Foundation, and the Brazilian Network of Human Milk Banks, released a statement providing guidance on Zika virus and breastfeeding. The document states that there is insufficient evidence to modify current breastfeeding practices [16].

Transmission of Zika virus via transfusion of infected blood or blood products remains a possibility. Three percent (3%) of asymptomatic blood donors (42/1 505) were found positive for Zika virus by PCR during the Zika virus outbreak in French Polynesia between November 2013 and February 2014, but there are no documented cases of infections via transfusion. The presence of a viable virus was detected in semen more than two weeks after recovery from an illness consistent with Zika virus infection [9,17]. Possible cases of sexual transmission of Zika virus have been reported [17,18].

*Aedes aegypti* is considered the most important vector for Zika virus transmission to humans, but other *Aedes* mosquitoes can also transmit Zika virus. *Aedes albopictus* has been identified as a potential vector of Zika virus [19,20].

More information on Zika virus disease can be found in the previous risk assessment and in the ECDC factsheet for health professionals [1-4].

Laboratory diagnosis mainly consists of detection of viral RNA genome through polymerase chain reaction (PCR), virus isolation, or the detection of specific Zika virus IgM or IgG antibodies through serological tests. More detailed information on laboratory diagnosis is provided in the Rapid Risk Assessment dated 25 May 2015 [2] as well as in the PAHO epidemiological alert of 1 December 2015 [21].

## Event background information

### Zika epidemic evolution

In 2013 and 2014, Zika virus outbreaks were notified in several islands of the Pacific region:

- French Polynesia reported an outbreak with 8 750 suspected cases of Zika virus infection, identified by the syndromic surveillance sentinel network of French Polynesia. There were 383 confirmed cases, and Zika virus disease may have been the cause of an estimated 32 000 patients presenting to healthcare facilities between October 2013 and April 2014 [22].
- Further spread to New Caledonia, the Cook Islands and later to Easter Island (Chile) has shown the propensity of this arbovirus to spread in the Pacific region, outside its usual geographical range in Africa and south-east Asia [23]. The virus found on Easter Island was closely related to the virus identified during the French-Polynesian outbreak, and cases were reported until June 2014 [24,25].

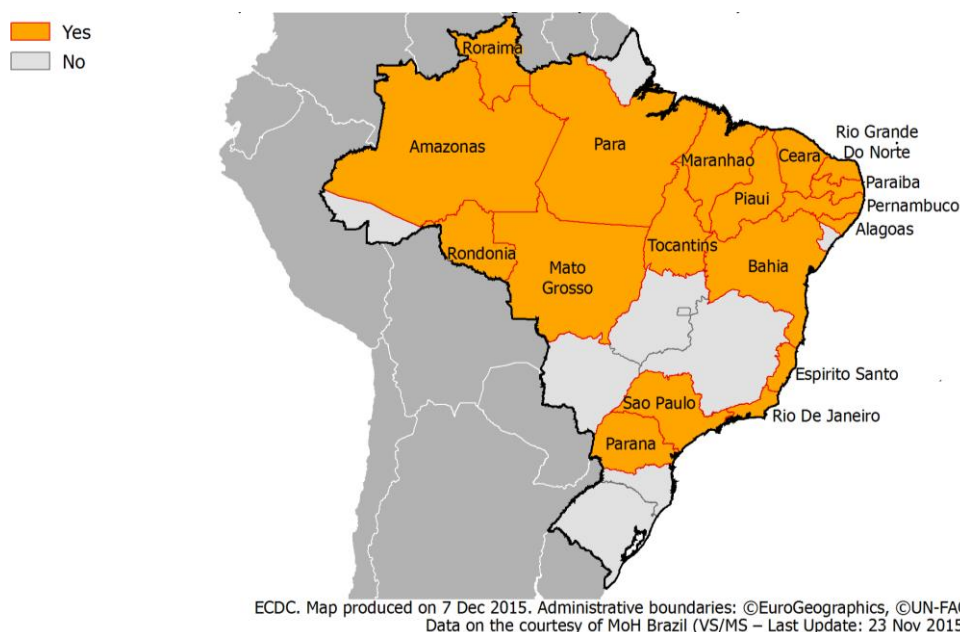
In 2015, autochthonous cases of Zika virus infection have been reported from Samoa and Solomon Islands (310 cases from February to May), New Caledonia (January to early August), Fiji (August), and at least one confirmed case in Vanuatu [26-28]. In 2015, Zika virus infections have spread to the Americas [25]:

- **Brazil:** Zika virus infections have been laboratory confirmed in 18 states in Brazil since February 2015. The following states and regions are affected: northeast (Bahia, Maranhão, Pernambuco, Rio Grande do Norte, Paraíba, Alagoas, Ceará and Piauí), north (Amazonas, Pará, Rondônia, Roraima and Tocantins), midwest (Mato Grosso), southeast (Espírito Santo, Rio de Janeiro and São Paulo) and south (Paraná), see Figure 1. The Brazilian National IHR Focal Point also reports that cases of rash illness without laboratory confirmation have been notified in the state of Sergipe. The samples were negative for dengue and chikungunya. Investigations in Sergipe by the Field Epidemiology Training Program (EpiSUS/FETP-Brazil) are ongoing. In May 2015, autochthonous transmission of Zika virus was confirmed in the states of Bahia and Rio Grande do Norte [29]. The surveillance model for Zika virus in Brazil is based on a sentinel network. Laboratory confirmation is done by RT-PCR in order to confirm autochthonous circulation as there are no standardised specific serological tests for Zika virus IgM or IgG antibodies available (cross-reaction with other flaviviruses especially with dengue fever).

In a study conducted by the Salvador Health Authorities, twelve health districts in Salvador City – the third-largest city in Brazil – reported 14 835 cases of exanthematous illness between 15 February and 25 June 2015, with a peak incidence in May and an overall attack rate of 5.5 cases/10 000 inhabitants [30]. The authors suggest that the outbreak was caused by Zika virus because the number of confirmed dengue cases did not vary substantially during the period; only 58 cases were diagnosed as chikungunya, and confirmed Zika virus infections occurred at the same time in other cities within metropolitan Salvador [30-32]. A phylogenetic analysis of serum samples from patients hospitalised in March at Santa Helena Hospital in Camaçari, Bahia, showed that the identified Zika virus sequences belonged to the Asian lineage and were 99% identical with one partial Zika virus envelope gene region from a Zika virus isolate from French Polynesia (KJ776791) [32].

According to preliminary estimates from the Brazilian ministry of health, between 440 000 to 1 300 000 cases of Zika virus infections may have occurred in 2015 in Brazilian states with laboratory-confirmed autochthonous cases of Zika virus [33]. As of 4 December 2015, the Brazilian ministry of health reported 9 300 suspected cases of chikungunya and approximately half a million probable cases of dengue to PAHO [34,35].

**Figure 1. States with laboratory-confirmed cases Zika virus disease, Brazil, 2015, as of 23 November 2015**



- **Colombia:** In September, the state of Bolívar reported nine confirmed autochthonous cases of Zika virus disease. As of week 47, Colombia has reported 578 confirmed and 3 700 suspected cases, from 26 of Colombia's 36 territorial entities [36].
- **El Salvador:** On 24 November, the IHR National Focal Point of El Salvador notified three confirmed autochthonous cases of Zika virus infection. On 3 December, the media reported 240 cases across the country [37].
- **Guatemala:** On 1 December, the media, quoting authorities, reported 17 suspected cases of Zika virus infection, 14 of which were among hospital employees. Blood samples were collected and sent to the US CDC for analysis [38]. So far, one of the samples has been reported as positive.
- **Mexico:** On 26 November, the Mexican ministry of health acknowledged three Zika virus cases, including two autochthonous cases reported from Nuevo León and Chiapas. The imported case had a recent travel history in Colombia [39].
- **Panama:** On 3 December, the local health authorities reported three autochthonous cases among residents of the district of Ailigandi, in the north-eastern province of Guna Yala. [40].
- **Paraguay:** On 27 November, Paraguay reported the confirmation of six Zika virus cases in the city of Pedro Juan Caballero, which borders Brazil, after an increase in the number of notified fever cases [41].
- **Venezuela:** On 27 November, the Venezuelan IHR National Focal Point notified seven Zika virus cases (autochthonous transmission is suspected), four of which were confirmed by RT-PCR [42].
- On 3 November 2015, the **Cape Verdean** ministry of health reported that 17 out of 64 blood samples sent for confirmation to Pasteur Institute in Dakar were positive for Zika virus. According to the ministry, approximately 1 000 suspected cases with symptoms consistent with Zika virus infection were recorded as of 1 November 2015 [43]. The overall distribution is reported in Figure 2 below (as of 4 December).

**Figure 2. Countries with reported confirmed autochthonous cases of Zika virus infection in 2015, as of 4 December**



*Note: Map does not indicate the extent of the autochthonous transmission in the countries.*

## Update on microcephaly and central nervous system malformations increase in Brazil

In October 2015, following reports of an unusual increase of cases of microcephaly among newborns in the state of Pernambuco, an analysis of data from the Brazilian live birth information system (SINASC) identified a significant increase in the number of microcephaly cases compared with previous years [44].

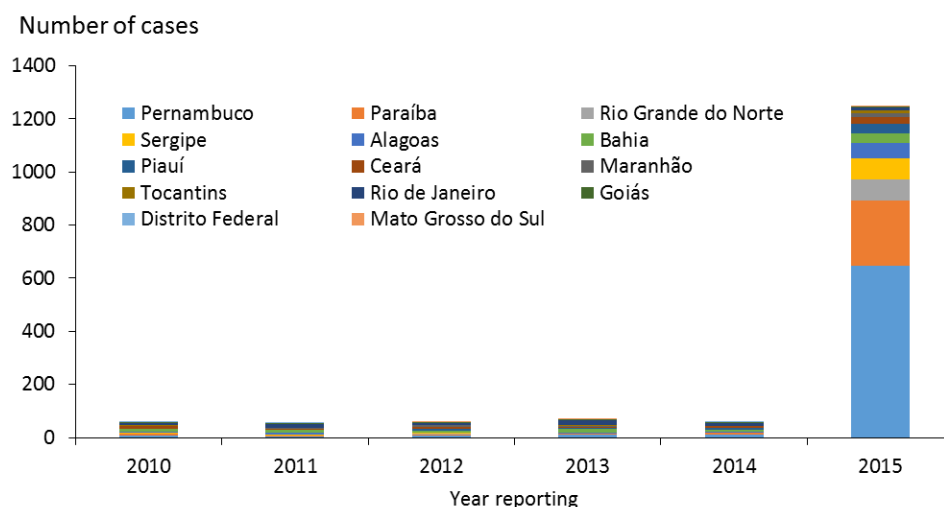
Possible links between Zika virus infection in pregnancy and microcephaly of the foetus have been under investigation since October 2015 when the Brazilian ministry of health reported an unusual increase in cases of microcephaly in the north-eastern states of Brazil [21]. On 11 November 2015, the Brazilian ministry of health declared a public health emergency in response to the dramatic increase over the expected incidence of microcephaly in Pernambuco state [45].

On average, between 150 and 200 children per year were born with microcephaly in Brazil between 2010 and 2014 (Figure 3 and Table 1). In 2015, as of 28 November, 1 248 suspected cases of microcephaly have been identified in 311 municipalities across 14 of the 26 states and one federal district of Brazil, of which 509 cases were reported between 21 and 28 November 2015 [46]. Pernambuco state has reported the highest number of cases (646), followed by the states of Paraíba (248), Rio Grande do Norte (79), Sergipe (77), Alagoas (59), Bahia (37), Piauí (36), Ceará (25), Rio de Janeiro (13), Maranhão (12), Tocantins (12), Goiás (2), Distrito Federal (1) and Mato Grosso do Sul (1) (see Figure 4) [47,48]. This is a significant increase compared to previous years (see Table 1) [46].

Brazilian health authorities have established an emergency operations centre for public health (COES, Centro de Operações de Emergências em Saúde Pública) and deployed rapid response teams to the affected states to support the investigations, provide guidance on the notification and surveillance processes, establish prenatal monitoring, and issue recommendations on prevention and control measures. The ministry of health of Brazil emphasises the importance of recommendations for pregnant women to avoid the consumption of alcohol, drugs, medications without prescription, and contact with people presenting with fever or infection. In addition, specific recommendations were issued relating to protection from mosquito bites, such as keeping doors and windows closed or screened, wearing trousers and long-sleeved shirts, and using repellents authorised during pregnancy. Clinical, laboratory and ultrasound analyses of pregnant women, mothers and newborns are being carried out.

PAHO/WHO published an epidemiological alert on the increase of microcephaly in the northeast of Brazil asking Member States to report similar events through the channels established under the International Health Regulations (IHR) [49]. On 1 December, PAHO/WHO issued an updated alert on neurological syndromes, congenital malformations, and Zika virus infection [49].

**Figure 3. Notified cases of microcephaly in Brazil from 2010 to 2015, with 14 states under investigation, as of 28 November 2015**



Baseline of notification of microcephaly for Brazil: 2010 (n=153), 2011 (n=139), 2012 (n=175), 2013 (n=167) and 2014 (n=147).

Adapted from [48]

**Table 1. Summary of number of microcephaly cases per 1 000 live births reported annually in the fourteen Brazilian states that investigate microcephaly; 2010–2014; 2015 data as of 28 November**

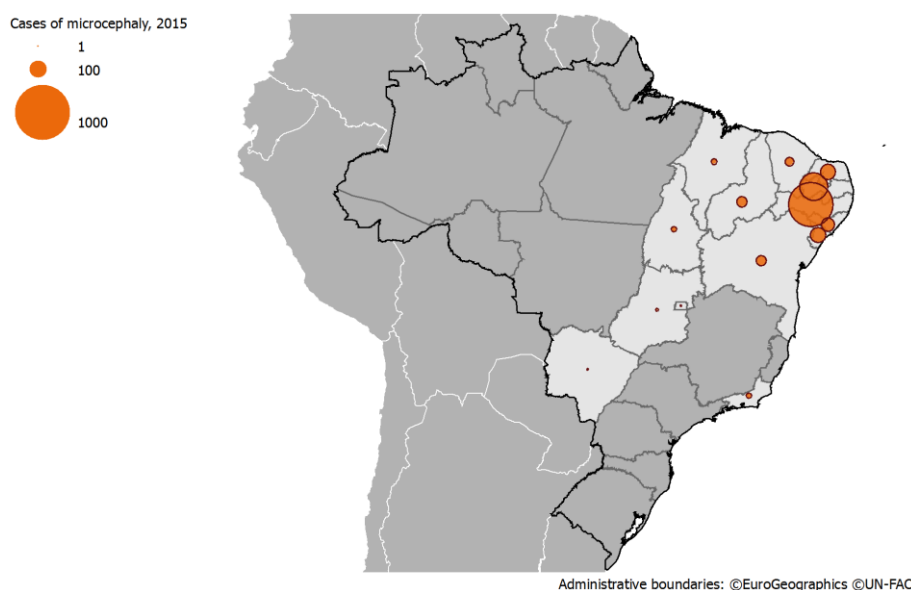
State	2009–2013 <sup>a</sup>	2010–2014 <sup>b</sup>		2015, as of 28 November		
	Yearly average number of live births (LB)	Yearly average number of microcephaly cases	Number of microcephaly per 1 000 LB	Number of microcephaly cases	Number of microcephaly cases per 1 000 LB*	Ratio between 2015/2010–2014
Pernambuco	140 264	8.6	0.06	646	4.61	77
Paraíba	47 998	4.2	0.09	248	5.17	57
Rio Grande do Norte	47 698	1.8	0.04	79	1.66	42
Sergipe	34 477	1.6	0.05	77	2.23	45
Alagoas	44 331	3.4	0.08	59	1.33	17
Bahia	211 660	10.6	0.05	37	0.17	3
Piauí	48 989	3	0.06	36	0.73	12
Ceará	128 112	6.6	0.05	25	0.2	4
Rio de Janeiro	219 876	12.4	0.06	13	0.06	1
Tocantins	24 586	1.2	0.05	12	0.49	10
Maranhão	119 069	3	0.03	12	0.1	3
Goiás	90 559	3	0.03	2	0.02	0.7
Distrito Federal	43 935	2.6	0.06	1	0.02	0.3
Mato Grosso do Sul	41 421	0.8	0.02	1	0.02	1
<b>Total</b>	<b>1 242 975</b>	<b>62.8</b>	<b>0.05</b>	<b>1248</b>	<b>1</b>	<b>20</b>

Adapted from [48]

\* The denominator used for this calculation is the average number of live births per year (2009–2013)

Data source: a) [50], b) [48]

**Figure 4. Reported cases of microcephaly in Brazilian states under investigation in 2015, as of 28 November**



*Note: Data for other states are unavailable.*

On 17 November, the Brazilian ministry of health reported the presence of Zika virus RNA in amniotic fluid samples collected from two pregnant women with foetal microcephaly from the state of Paraíba. This finding was confirmed by RT-PCR, at the Flavivirus laboratory of the Oswaldo Cruz Institute [51]. The two mothers had symptoms compatible with Zika virus disease at gestation weeks 18 and 19. Foetal Zika virus infection was confirmed through detection of Zika virus genome by RT-PCR in amniotic fluid from the two children born with microcephaly. Ultrasonography done at gestation week 20 revealed calcifications in the foetuses' brains, and a repeat scan at gestation week 28 confirmed the diagnosis of microcephaly. Urine and serum samples from the mothers were negative for Zika virus genome detection at gestation week 28 but amniocenteses were positive, with a viral load 10 000 times higher than what is normally found in blood from adults with acute infection and exanthema.

On 28 November 2015, the Brazilian ministry of health reported the presence of Zika virus genome in the blood and tissue samples of a baby from the state of Pará with microcephaly. The newborn presented with microcephaly and other congenital anomalies and died within five minutes of being born. The confirmation of the presence of the viral genome was provided by the Evandro Chagas Institute, the national reference laboratory for arboviruses in Belém, Pará [21].

On 24 November 2015, the health authorities of French Polynesia reported an unusual increase of at least 17 cases of central nervous system malformations in foetuses and infants during 2014–2015, coinciding with the Zika outbreaks in the French Polynesian islands. Investigations are still ongoing. Based on the temporal correlation of these cases with the Zika epidemic, the health authorities of French Polynesia hypothesise that Zika virus infection may be associated with these abnormalities if mothers are infected during the first or second trimester of pregnancy [3].

## Update on Guillain–Barré syndrome

During the Zika virus outbreak in French Polynesia with 8 750 suspected cases, 74 patients presented with neurological syndromes or autoimmune syndromes following an illness with symptoms compatible with Zika virus infection in previous days. Of these, 42 were diagnosed as Guillain–Barré syndrome, 37 of which had presented with a previous viral syndrome [3,22]. Investigations are still ongoing in Brazil and French Polynesia to establish if Zika virus infection increases the risk of developing Guillain–Barré syndrome.

In Brazil, 121 cases of neurological manifestations and Guillain–Barré syndrome (GBS) were notified. All 121 cases had a history of rash illness and had been notified in north-eastern states between January and July 2015 [52]. Investigations are ongoing to assess a possible association between Zika virus infection and neurological manifestations and GBS [25].

According to the PAHO/WHO alert on 1 December 2015, 76 patients with neurological syndrome had been identified up to 13 July, the majority in the state of Bahia: 42 cases were classified as GBS, five were diagnosed as other neurological conditions, and 29 were either discarded or remain under investigation. Among patients with GBS, 62% (26/42) had symptoms consistent with a Zika virus infection preceding the onset of the neurological symptoms [21].

According to news reports quoting the Brazilian ministry of health on 1 December, 28 cases of GBS reported in Sergipe State were potentially linked to dengue or Zika infection [53]. According to media reports, seven cases of Guillain–Barré syndrome (GBS) reported from Pernambuco State last week were linked to Zika virus infection [54].

## Fatalities potentially linked to Zika virus infection

On 30 November 2015, the COES (Centro de Operações de Emergências em Saúde Pública sobre microcefalias) reported three deaths attributed to Zika virus infection:

- A newborn with congenital anomalies (microcephaly, fetal anasarca and polyhydramnios) who died within the first five minutes of life was tested positive for Zika virus genome in Ceara State the 18 of November. Analysed samples were blood and tissue samples.
- An adult male with co-morbidities and immunosuppressive treatment. Zika virus RNA was identified in blood, brain, liver, spleen and viscera pool (kidney, lung and heart). RT-PCR for dengue genome detection was negative. Results of the other tests performed are not reported (chikungunya, West Nile fever, Saint Louis encephalitis, and yellow fever).
- A 16-year-old female from the city of Benevides (state of Pará) with onset of symptoms on 29 September 2015 (headache, nausea and petechiae) and notification on 6 October 2015. The patient was initially thought to have dengue fever, however further laboratory testing confirmed Zika virus infection by RT-PCR on a blood sample collected seven days after onset of symptoms. Further laboratory tests are ongoing (dengue fever and chikungunya infection).

Seven deaths were reported with a potential link to Zika virus infection and are now being investigated by the Brazilian ministry of health in Rio Grande do Norte (n=5), Ceará (n=1) and Piauí (n=1) [47].

## ECDC threat assessment for the EU

### Risk of Zika virus importation and transmission in the continental EU

Few travel-associated cases of Zika virus infections have been reported in the EU. Infections followed exposure in Asia or in French Polynesia [55-58]. With the spread of the Zika virus epidemic in the Americas, the likelihood of travel-related cases of Zika virus infection in the EU is increasing.

The *Aedes albopictus* mosquito species is established in many parts of the EU, primarily around the Mediterranean [59]. Onward transmission from imported cases within the continental EU is possible because *Aedes albopictus* is probably a competent vector for the transmission of Zika virus, even though this has not been confirmed for European mosquito populations [19,20]. The risk for transmission of Zika virus infections is extremely low in the EU during winter season as the climatic conditions are not suitable for the activity of potential vectors.

### Risk of Zika virus importation and transmission for EU Overseas Countries and Territories and Outermost Regions

The probability of introduction of the virus from Zika virus-affected countries to EU Overseas Countries and Territories and EU Outermost Regions, especially in South America and in the Caribbean, has increased since the rapid risk assessment published on 25 May 2014 [2] as the epidemic is currently spreading in South America. Considering the presence of *Aedes aegypti* and *Aedes albopictus* – two competent vector species in these Overseas Countries, Territories and Outermost Regions – the establishment of local transmission is possible once the virus is introduced. This risk also includes Madeira because of its close relationship and intense trade and travel with Brazil and Cape Verde, where Zika virus is currently circulating, and the presence of competent vectors (*Aedes aegypti*).



## Risk of Zika virus infection for travellers to affected regions

Travellers to countries where Zika virus is circulating are at risk of developing the disease through mosquito bites.

As neither treatment nor vaccines are available, prevention is based on personal protection measures similar to the ones against dengue and chikungunya. *Aedes* mosquitoes bite during the day as well as in the late afternoon and early evening.

## Risk of Zika virus infection associated with blood donations

According to Musso et al., 42 of 1 505 (3%) blood donors in French Polynesia, although asymptomatic at the time of blood donation, were found positive for Zika virus genome by PCR, supporting a potential risk of transfusion-derived transmission [9]. Transfusion-transmitted Zika virus infection has not been reported. However, transmission is possible through blood donated by viraemic, symptomatic residents or travellers returning from affected areas [9,60,61]. Therefore, EU blood authorities may consider a temporary deferral from blood donation of persons with a travel history to affected areas (14 days as used for dengue).

Blood safety strategy in affected areas entails the deferral of donors with a diagnosis of Zika infection for 28 days from cessation of disease symptoms, pathogen inactivation of platelets and fresh frozen plasma, and enhanced post-donation reporting from donors who develop symptoms compatible with Zika fever [62].

In areas endemic for *Aedes* species, a preparedness plan to respond to future outbreaks of Zika virus infection should consider to include emergency plans to sustain blood supply.

## Potential association between Zika virus infection and severe outcomes

Epidemiological data available as of November 2015 indicate, on average, a twenty-fold increase (range 0–77) in the incidence of microcephaly among newborns in the fourteen Brazilian states with Zika virus circulation that investigate microcephaly.

Initial reports of increased numbers of newborns with a low head circumference detected in the Brazilian live birth information system were a strong alert signal.

The case definition of microcephaly used so far stated a head circumference at birth of 33 centimetres or below (newborns after 37–43 weeks of gestation). However, the use of a single head circumference cut-off point for male and female newborns is not a very effective tool to assess the extent of microcephaly and establish a possible link with central nervous malformations in newborns. Investigations and follow-ups of newborns with a low head circumference will allow a more precise quantification of the malformations.

According to a protocol published on 8 December 2015, the Brazilian authorities are implementing a new case definition for microcephaly based on a head circumference for newborns of 32 centimetres or below. The new protocol will result in a decrease in the number of newborns suspected of microcephaly. Previously reported cases of microcephaly with head circumferences of up to 33 centimetres will remain under surveillance and may be reclassified [33].

Zika virus genome has been detected in the blood and tissue samples of a baby from the state of Pará. The newborn presented with microcephaly and other congenital anomalies and died. In addition, foetal Zika virus infection has been confirmed through detection of Zika virus genome by RT-PCR in the amniotic fluid of two children born with microcephaly. These observations support the conclusion of the rapid risk assessment of 24 November that a causal association between microcephaly in newborns and Zika virus infection during pregnancy is plausible [3]. However, more evidence is needed to confirm this association.

On 1 December, the PAHO/WHO issued an epidemiological alert noting that according to the preliminary analysis of the investigation conducted by the Brazil health authorities, the risk of microcephaly or congenital anomalies in newborns that is possibly associated with Zika virus infection is likely to be greatest in the first trimester of pregnancy.

In addition, investigations are still ongoing regarding a possible association between Zika virus infection and Guillain–Barré syndrome (GBS) in Brazil and French Polynesia. As of 1 December 2015, three additional fatal cases of Zika virus disease have been reported by Brazil.

In conclusion, there is limited but increasing knowledge about Zika virus infection in humans [63,64]. The disease symptoms are usually mild and last for 2 to 7 days. However, important uncertainties remain about disease complications, genetic susceptibility and levels of risk for pregnant women, newborns or patients presenting with specific co-morbidities. The spread of Zika virus infections to South, Central and North America constitutes a significant development in the epidemiology of this emerging vector-borne disease.

## Conclusions and options for mitigation

The Zika virus outbreak in the Americas and the South Pacific is evolving rapidly, and its spread is likely to continue as the vector species *Aedes aegypti* and *Aedes albopictus* are widely distributed there. While a significant increase in the number of newborns presenting with a low head circumference seems established in the north-eastern states of Brazil, the magnitude of the increase cannot be precisely estimated. Similarly, a link with Zika virus infection cannot be confirmed until the ongoing investigations are completed.

In the light of the current disease trend – and the possible association with severe complications – public health authorities in EU/EEA Member States should consider the following mitigation options:

- Enhance vigilance towards the detection of imported cases of Zika virus infection in EU Member States, EU Overseas Countries and Territories, and EU Outermost Regions, in particular where vectors or potential vectors are present, in order to reduce the risk of autochthonous transmission.
- Strengthen laboratory capacity to confirm suspected Zika virus infections in the European region in order to differentiate Zika virus infections from other arboviral infections (e.g. dengue, chikungunya).
- Blood safety authorities should consider the deferral of donors with a relevant travel history to areas with active Zika virus transmission, in line with measures defined for dengue virus.
- Increase awareness of clinicians and travel health clinics about the evolution of the Zika virus outbreak and the endemic areas so that they can include Zika virus infection in their differential diagnosis for travellers from those areas. Fever and/or macular or papular rash not attributable to dengue or chikungunya infection among travellers returning from areas currently experiencing a Zika virus outbreak should be considered indications for further investigation of Zika virus infection.
- Advise residents and travellers visiting affected areas, particularly pregnant women, to take individual protective measures to prevent mosquito bites all day round as Zika virus disease, chikungunya and dengue are transmitted by a daytime-biting mosquito. Consequently, protective measures should be taken, especially during the day.
- Ensure that Zika virus-infected patients in areas with *Aedes* mosquitoes avoid getting bitten during the first week of illness (mosquito net, screened doors and windows as recommended by WHO/PAHO).
- Increase awareness among health professionals who provide prenatal care of the possible association of Zika virus and microcephaly and adapt prenatal monitoring in accordance with the level of exposure to the vector.

## Information for travellers to areas with circulation of Zika virus disease

- Travellers visiting countries where Zika virus is circulating should be made aware of the ongoing outbreak of Zika virus infection.
- Travellers visiting these countries should use personal preventive measures based on protection against mosquito bites. As *Aedes* mosquitoes bite during the day, both indoors and outdoors, personal protection measures should be applied all day long, especially during the hours of highest mosquito activity (mid-morning, late afternoon to dusk).
- Personal protection measures to avoid mosquito bites should include the following:
  - Using mosquito repellents in accordance with the instructions indicated on the product label. DEET\*-based repellent use is not recommended in children under three months of age but can be used in concentrations up to 50% in pregnant women.
  - Wearing long-sleeved shirts and long pants, especially during the hours of highest mosquito activity.
  - Using insecticide-treated mosquito nets is essential if accommodations are not adequately screened or air conditioned.
- Travellers that are pregnant, have immune disorders or severe chronic illnesses, or are accompanied by young children should consult their doctor or seek advice from a travel clinic before travelling in order to receive recommendations on the use of repellents and other preventive measures.
- Travellers showing symptoms compatible with dengue, chikungunya or Zika virus disease within three weeks after returning from an affected area should contact their healthcare provider.
- Pregnant women who have travelled to areas with Zika virus transmission should mention their travel during antenatal visits in order to be assessed and monitored appropriately.

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\* DEET: N,N-Diethyl-meta-toluamide or diethyltoluamide, a common active ingredient in insect repellents.

## References

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